

more attention should be paid to patients' views to increase treatment adherence.

Qualitative studies have also permitted to better understand differences in access to total knee or hip arthroplasties among patients with knee or hip OA and motives of satisfaction or dissatisfaction of patients after these surgical interventions.

Finally, qualitative research will probably lead to consider concepts differing from disability or HRQoL such as expectations, needs, fears and beliefs and help to develop accurate measure tools to assess these concepts.

I-8

THE ROLE OF MIR-140 IN OA PATHOGENESIS

H. Asahara^{1,2}. ¹The Scripps Res. Inst., La Jolla, CA, USA; ²Tokyo Med. and Dental Univ. and Natl. Res. Inst. for Child Hlth. and Dev., Tokyo, Japan

Purpose: Osteoarthritis (OA) is the most prevalent disorder of synovial joints, characterized by focal areas of articular cartilage destruction. MicroRNAs (miRNAs) are a family of ~22-nucleotide (nt) noncoding RNAs that are evolutionarily conserved and regulate gene expression by posttranscriptional mechanisms. miR-140 is highly expressed in chondrocytes, however its function has not yet been elucidated.

Methods and Results: To examine the role of miR140 in vivo, we generated miR140 null mice. During embryogenesis and at neonatal stage, skeletal formation of miR140 null mice is not significantly disturbed compared with wild type mice. Postnatal growth of limbs and body of null mice is slightly significantly repressed compared with wild-type.

In null miR140 mice knee articular cartilage we observed spontaneous onset of osteoarthritis at the age of 8 months.

To test the function of miR-140 in articular cartilage, we performed microarray for mRNA expression with articular cartilage from wild type and miR-140 null mice and on chondrocytes transfected with miR-140. Among the mRNAs most highly increased in miR140 null mice was ADAMTS-5, a critical cartilage degradation enzyme in osteoarthritis pathogenesis. ADAMTS-5 is also a strong miR-140 candidate as predicted from Target scan bioinformatics data-base. ADAMTS-5 expression is significantly increased in chondrocytes from miR-140 null mice. Consistent with this, GAG loss in articular cartilage was significantly increased in miR140 null mice. Overexpression of miR-140 in chondrocytes from miR-140 null mice decreased the expression of ADAMTS-5. Furthermore, reporter construct carrying ADAMTS-5 3' UTR was also inhibited by miR-140 overexpression.

Conclusions: These data indicate that ADAMTS-5 is directly inhibited by miR-140 and that loss of miR-140 causes catabolic effect on cartilage homeostasis and subsequent osteoarthritis, at least in part, via regulating ADAMTS-5.

I-9

HAND OA: A DISEASE IN NEED OF TREATMENT

K. Dziedzic. Arthritis Res. UK Primary Care Ctr. Keele Univ., Keele, United Kingdom

Hand osteoarthritis is one of the commonest forms of osteoarthritis and until recent years there has been limited research and a general feeling that nothing can be done for people with hand OA. The talk will have an emphasis on primary care where most people present and where there is a gap between what patients could be offered and what patients receive [1].

The presentation will describe hand OA not as a single disease but as a group of complex conditions [2] ranging a syndrome of joint pain accompanied by functional limitation, or a condition defined by the presence of features and severity of symptoms (ACR criteria) [3], to highly characterised subsets of radiographic hand OA [4]. The presentation in particular will draw on findings from three large cohorts of adults 50 years and over studied in the North West Midlands in the UK (n=30,000) (Norstop1 [5], CAS-HA [6], Smooth [7]).

The prevalence of hand OA and impact on hand pain and functional decline over three years will be described, along with consultation for hand pain and hand OA in primary care using survey data and consultation records. Hand OA as an important marker of OA in the person will be highlighted.

Using OARS recommendations for the design and conduct of trials in hand OA [8] patients in need of treatment will be defined and the uptake

of treatment by eligible individuals will be reported using a study of hand exercises and joint protection as an example [7].

Reference(s)

- [1] Hill S, Dziedzic KS, Ong BN. The functional and psychological impact of hand osteoarthritis. *Chronic Illn.* 2010 Jun;6(2):101–10. Epub 2010 May 5
- [2] Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, Dincer F, Dziedzic K, Hauselmann HJ, Kaklamanis P, Kloppenburg M, Lohmander LS, Maheu E, Martin-Mola E, Pavelka K, Punzi L, Reiter S, Smolen J, Verbruggen G, Watt I, Zimmermann-Gorska I; ESCISIT. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. *Ann Rheum Dis.* 2009 Jan;68(1):8–17. Epub 2008 Feb 4. Review.
- [3] Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Gray R: The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum* 1990, 33(11):1601–1610.
- [4] Marshall M, van der Windt D, Nicholls E, Myers H, Hay E, Dziedzic K. Radiographic hand osteoarthritis: patterns and associations with hand pain and function in a community-dwelling sample. *Osteoarthritis Cartilage.* 2009 Nov;17(11):1440–7. Epub 2009 May 20.
- [5] Dziedzic K, Thomas E, Hill S, Wilkie R, Peat G, Croft PR. The impact of musculoskeletal hand problems in older adults: findings from the North Staffordshire Osteoarthritis Project (NorStOP). *Rheumatology (Oxford).* 2007 Jun;46(6):963–7. Epub 2007 Feb 28.
- [6] Myers H, Nicholls E, Handy J, Peat G, Thomas E, Duncan R, Wood L, Marshall M, Tyson C, Hay E, Dziedzic K: The Clinical Assessment Study of the Hand (CAS-HA): a prospective study of musculoskeletal hand problems in the general population. *BMC Musculoskelet Disord* 2007, 8:85.
- [7] Dziedzic KS, Hill S, Nicholls E, Hammond A, Myers H, Whitehurst T, Bailey J, Clements C, Whitehurst DGT, Jowett S, Handy J, Hughes RW, Thomas E, Hay EM. Self management, joint protection and exercises in hand osteoarthritis: a randomised controlled trial with cost effectiveness analyses *BMC Musculoskelet Disord* 2011 in press
- [8] Maheu E, Altman RD, Bloch DA, Doherty M, Hochberg M, Mannoni A, Punzi L, Spector T, Verbruggen G, Osteoarthritis Research Society International Hand OA Task Force, Carr A, Cicuttini F, Dreiser RL, Haraoui BP, Hart D, Pelletier JP, Ramonda R, Rovati L: Design and conduct of clinical trials in patients with osteoarthritis of the hand: recommendations from a task force of the Osteoarthritis Research Society International. *Osteoarthritis Cartilage* 2006, 14(4):303–322.

I-10

WHAT'S WRONG WITH ANIMAL MODELS OF PAIN?

J. Mogil. McGill Univ., Montreal, QC, Canada

Recent decades have seen an explosion in our understanding of the molecular and cellular underpinnings of pain, but virtually none of this knowledge has resulted in new clinical therapies. Many pain researchers believe that the problem may lie in the existing animal models of pain, which are reliable but much more complex and subtle than is commonly realized, and of questionable clinical relevance. Most basic science studies of pain continue to rely on the measurement of reflexive, evoked hypersensitivity responses after artificial neuropathic or inflammatory injuries, whereas clinical pain in humans features much spontaneous pain and an important cognitive and emotional overlay. In addition to the disconnect between clinical symptoms and animal measures, there is a disconnect between the clinical epidemiology of pain and the types of pain being modeled in animals. We have recently attempted to develop an "ethological" approach to animal models of common pain pathologies, involving systematic and rigorous analysis of videotaped spontaneous mouse behaviors. I will talk about some recent successes in our laboratory, involving migraine, vestibulodynia, and the development of a facial expression-based pain scale for the mouse.